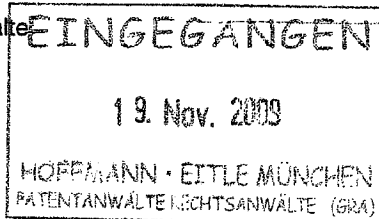




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18.11.09

Reference 117 831 a/jme	Application No./Patent No. 05727997.8 - 1222 / 1736173 PCT/JP2005006320
Applicant/Proprietor Two Cells Co., Ltd, et al	

Communication

The European Patent Office herewith transmits as an enclosure the supplementary European search report under Article 153(7) EPC for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

- ☒ 1 additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

Refund of the search fee

If applicable under Article 9 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





**SUPPLEMENTARY
PARTIAL EUROPEAN SEARCH REPORT**

Application Number

which under Rule 63 of the European Patent Convention EP 05 72 7997 shall be considered, for the purposes of subsequent proceedings, as the European search report

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	AKITA SADANORI ET AL: "Cranial bone defect healing is accelerated by mesenchymal stem cells induced by coadministration of bone morphogenetic protein-2 and basic fibroblast growth factor." WOUND REPAIR AND REGENERATION : OFFICIAL PUBLICATION OF THE WOUND HEALING SOCIETY [AND] THE EUROPEAN TISSUE REPAIR SOCIETY 2004 MAR-APR, [Online] vol. 12, no. 2, 20 February 2004 (2004-02-20), pages 252-259, XP002553495 ISSN: 1067-1927 Retrieved from the Internet: URL: http://www3.interscience.wiley.com/cgi-bin/fulltext/118800000/PDFSTART [retrieved on 2009-11-02] * the whole document *	1-15	INV. A61K45/00 A61K31/728 A61K35/12 A61K38/00 A61K38/22 A61K38/27 A61K38/46 A61L27/00 A61P1/02 A61P9/10 A61P19/00 C12N5/08 C12N5/06
			TECHNICAL FIELDS SEARCHED (IPC)
			C12N A61K
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
INCOMPLETE SEARCH			
The Search Division considers that the present application, or some or all of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for the following claims:			
Claims searched completely :			
Claims searched incompletely :			
Claims not searched :			
Reason for the limitation of the search: see sheet C			
Place of search The Hague		Date of completion of the search 3 November 2009	Examiner Manu, Dominique
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			
T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

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EPO FORM 1503 03.02 (P04E20)

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 05 72 7997

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A	FIEDLER JÖRG ET AL: "BMP-2, BMP-4, and PDGF-bb stimulate chemotactic migration of primary human mesenchymal progenitor cells." JOURNAL OF CELLULAR BIOCHEMISTRY 2002, vol. 87, no. 3, 2002, pages 305-312, XP002553496 ISSN: 0730-2312 * the whole document *	1-15	
A	WO 2004/007697 A (YISSUM RES DEV CO [IL]; ASLAN HADI [IL]; GAZIT DAN [IL]; GAZIT ZULMA []) 22 January 2004 (2004-01-22) * paragraph [0039] - paragraph [0043] *	1-15	
T	OZAKI YOSHIE ET AL: "Comprehensive analysis of chemotactic factors for bone marrow mesenchymal stem cells." STEM CELLS AND DEVELOPMENT FEB 2007, vol. 16, no. 1, February 2007 (2007-02), pages 119-129, XP008114175 ISSN: 1547-3287 * the whole document *	1-15	TECHNICAL FIELDS SEARCHED (IPC)



INCOMPLETE SEARCH
SHEET C

Application Number
EP 05 72 7997

Claim(s) searched completely:

-

Claim(s) searched incompletely:

1-15

Claim(s) not searched:

-

Reason for the limitation of the search:

Present claims 1-6, 8-11 and 13-15 relate to an agent/factor or a transplant which has a given desired property or effect, namely which is capable of enhancing the migration and accumulation of administered mesenchymal stem cells (MSC) in an injured tissue and/or suppressing the diffusion of administered MSC from an injured site (i.e. a chemoattractant for MSC). However, the description does not provide support and disclosure within the meaning of Articles 84 and 83 EPC for any such agent/factor or transplant having the said property or effect and there is no common general knowledge of this kind available to the person skilled in the art. This non-compliance with the substantive provisions is such that a meaningful search of the whole claimed subject-matter of the claim could not be carried out (Rule 63 EPC and Guidelines B-VIII, 3). The search of claims 1-6, 8-11 and 13-15 has to be restricted to the specifically disclosed agents having the desired property or effect as listed in claims 8 and 12 and in the description on paragraphs [0047] and [0053] for instance, as well as to the broad concept of MSC chemoattractants and chemotaxis.

It is not clear whether claims 1-4 and 7 refer to a standard product claim or if it is to be construed as a product for use in therapy as in dependent claim 5 (Article 84 EPC). The disease/pathology to be treated is not clearly indicated in claims 1-5, 7-10 and 12-15 contrary to Article 84 EPC (see Guidelines C-IV, 4.8). Also, with respect to claims 1-15, it is not clear whether MSC are also included in the scope of the claims as part of the treatment, as would be suggested by the content of claims 2 and 9 (Article 84 EPC). For the purpose of the search it was considered that claims 1-15 referred to a factor and MSC for use in therapy.

The above restrictions in scope were taken into account when assessing the unity of the present application



Application Number

EP 05 72 7997

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

☒ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-15 (partially)

Use of EGF in combination with MSC in therapy or for the
preparation of a medicament for regeneration therapy

2. claims: 1-15 (partially)

Same with HB-EGF

3. claims: 1-15 (partially)

Same with TGF-alpha

4. claims: 1-15 (partially)

Same with thrombin

5. claims: 1-15 (partially)

Same with PDGF

6. claims: 1-15 (partially)

Same with FGF

7. claims: 1-15 (partially)

Same with Hyaluronic acid

8. claims: 1-15 (partially)

Same with IGF

9. claims: 1-15 (partially)

Same with HGF

The present application, relates to the use of an agent capable of acting as a chemoattractant for administered MSC in therapy. The single general concept which can be identified a priori as linking the claimed inventions is the use of factors, capable of stimulating MSC chemotaxis to promote MSC therapeutic action.

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

Sandanori et al. (D1) discloses the co-administration of BMP-2 and bFGF together with MSC in the treatment of bone defects (the whole document). Although, in D1, bFGF is not shown to effect MSC chemotaxis, this is an implicit feature of bFGF, as shown in the present application itself. Although the mechanism of action of the different factors is characterised in the present application, it does not lead to the healing of a different pathology. It follows that the above-identified single general concept is not novel and inventive and cannot be regarded as the single general inventive concept as set out in Rule 44 EPC and Article 82 EPC.

In view of D1 the objective problem to be solved by the present application can be regarded as the provision of further agents to promote the therapeutic action of MSC. In this respect every agent/factor represents a separate solution i.e. a separate invention.

Since the application only discloses a limited number of agents/factors with MSC chemotactic characteristics and since no other agents were known to the skilled person at the time of the invention, the different inventions could only be split up based on the agents/factors disclosed in the application:

- 1) Use of EGF in combination with MSC in therapy or for the preparation of a medicament for regeneration therapy (claims 1-15, partially)
- 2) Same with HB-EGF (claims 1-15, partially)
- 3) Same with TGF- alpha (claims 1-15, partially)
- 4) Same with thrombin (claims 1-15, partially)
- 5) Same with PDGF (claims 1-15, partially)
- 6) Same with FGF (claims 1-15, partially)
- 7) Same with Hyaluronic acid (claims 1-15, partially)
- 8) Same with IGF (claims 1-15, partially)
- 9) Same with HGF (claims 1-15, partially)

No other technical features could be identified which would form a relationship between the separate inventions and which could be considered as special technical feature in the sense of Rule 44 EPC.

If ever the single general concept was to become chemotactic factors for MSC, this concept is already disclosed in Fiedler et al. (D2), and the application would still be considered to lack unity.

In accordance with Rule 164(1) EPC the supplementary search report has been drawn up on those parts of the application which relate to the invention, or group of inventions, first mentioned in the claims, i.e. invention 1.

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 05 72 7997

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

03-11-2009

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004007697 A	22-01-2004	AU 2003242976 A1	02-02-2004
		CA 2493871 A1	22-01-2004
		EP 1551955 A2	13-07-2005
		JP 2005532810 T	04-11-2005
		US 2005249731 A1	10-11-2005
<hr/>			

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